REMARKS

I. Introduction

Receipt of a final Office Action dated February 7, 2007 is acknowledged. In the Action, claims 28-40, 42-45, and 47-59 are rejected allegedly for failing to meet the written description requirement, and as allegedly obvious over Liversidge *et al.*, US Patent No. 5,145,684 ("Liversidge"), in view of Folke Moren, AEROSOLS IN MEDICINE, PRINCIPLES, DIAGNOSIS AND THERAPY, Chapter 13, pp. 321-350, Elsevier Science Publisher (1993) ("Moren"), or in view of A.R. Gennaro, REMINGTON'S PHARMACEUTICAL SCIENCES, 17TH ED., Chapter 93, pp. 1670-77 (1985) ("Gennaro") and Dieter Kohler, AEROSOLS IN MEDICINE, PRINCIPLES, DIAGNOSIS AND THERAPY, Chapter 12, pp. 303-19, (1993) ("Kohler").

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

II. Status of the Claims

In this Amendment, claims 28 and 44 are amended and claim 45 is cancelled. Upon entry of this amendment, claims 28-40, 42-44, and 47-59 are pending and under examination.

It is acknowledged that the foregoing amendments are submitted after final rejection. However, because the amendments do not introduce new matter or raise new issues, and because the amendments either place the application in condition for allowance or at least in better condition for appeal, entry thereof by the Examiner is respectfully requested.

III. Rejection of the Claims Under 35 U.S.C. § 112, first paragraph

Claims 28-40, 42-45, and 47-50 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to meet the written description requirement. In particular, the claims are rejected because "Applicant had no possession at the time this application was filed of claimed 'method of delivering' and the steps as claimed . . . and method of treating respiratory illness such as AIDS, AIDS-related pneumonia, respiratory distress syndrome and various others listed in claim 44." Office Action at 4. Applicants respectfully disagree.

The claims are directed to a delivery method and not a method of treatment. The claimed delivery method comprises aerosol particles less than about 50 μm, and a therapeutic agent that is submicron sized. This is described throughout the specification. See, for example, page 2-3 of the originally filed specification. As such, it is not clear which aspect of the claim fails to meet the written description requirement.

In addition claim 1 as amended recites a droplet particle size of less than about 10 microns, thus rendering the rejection moot. Support for this amendment can be found in the background section of the invention.

The Office also stated that because claim 37 is directed to a number of therapeutic agents, and "[a]ll the therapeutic agents as in claim[s] 28 and 37 cannot have the same mode of action, effective doses, properties and activities" a complete study of the effective dosages, specific delivery and treatment are required. Office Action at 6. The agents described in claim 37, however, are the therapeutic agents that can be formulated for the claimed delivery method recited in claim 28 and that claim is not directed to a method of treatment. Accordingly, Applicants need not demonstrate the efficacy, treatment, etc. of the therapeutic agents of claim 37 because Applicants are not claiming those agents for treatment. The agents of claim 37 share the characteristic of being poorly soluble. The present invention describes methods of delivering poorly soluble active agents, whereas prior art delivery methods of these agents are inefficient.

In addition, claim 44 as amended does not recite AIDS or AIDS related pneumonia Withdrawal of rejection is respectfully requested.

IV. Rejection of the Claims Under 35 U.S.C. § 103

Claims 28-40, 42-45 and 47-59 are rejected under 35 U.S.C. § 103 as allegedly obvious over (1) Liversidge, in view of Folke Moren, and (2) Liversidge, in view of Gennaro and Dieter Kohler. Applicants respectfully traverse these grounds of rejection.

The Supreme Court recently reaffirmed the Graham factors for determining obviousness in *KSR Int'l Co. v. Teleflex Inc.* (No. 04-1350) (U.S., April 30, 2007). The

Graham factors, as outlined by the Supreme Court in *Graham et al. v. John Deere Co. of Kansas City et al.*, 383 U.S. 1 (1966), are: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the claimed invention and the prior art; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary consideration. The Supreme Court held that the proper inquiry for determining obviousness is whether the improvement is more than the predictable use of prior art elements according to their established functions. The Court noted that it is "*important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] element" in the manner claimed*, and specifically stated:

> [o]ften, it will be necessary . . . to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit.

KSR Int'l Co. v. Teleflex Inc., slip op. at 14 (emphasis added).

As discussed below, the differences between the prior art and the present application are so substantial, that the cited art cannot render the claimed invention obvious.

A. *Liversidge in view of Folke Moren*

Claims 28-40, 42-45 and 47-59 are rejected over Liversidge, in view of Folke Moren because "[i]t would have been obvious . . . to prepare the method of delivering an aerosol to lungs as claimed by the combined teachings of the two references cited above for the treatment of respiratory diseases by using aerosols because Liversidge et al teaches the average particle size, surface modifier, and all other limitations of the presently claimed invention and Moren teaches aerosols and delivery to respiratory tract using poorly soluble drugs such as steroids." Applicants respectfully disagree.

Moren describes some aqueous systems but teaches that one must choose a form of the drug that is soluble in water. *See*, Moren at section 4.1.1, page 340. In other words,

Moren provides that in order for aqueous aerosols to be effective, the drug should be in solution. Furthermore, Moren states that a water soluble form of the drug should be used, and that it may be necessary to adjust the formulation to achieve adequate solubility by, for example, (1) changing the pH, (2) adding a cosolvent, (3) adding a surfactant to form micelles, or (4) forming inclusion complexes. But Moren points out that there are disadvantages to these approaches, such as changes in viscosity and surface tension (which affect aerosol generation), increases or decreases in the liquid evaporation rate (which will affect droplet size), irritation to mucosa, coughing, bronchospasm, and lack of drug availability from micelles. Moreover, Moren teaches that the probability of success when trying to aerosolize a suspension is quite low because of problems with physical stability, lack of redispersion, accuracy of dose, and problems with fragmenting the liquid.

Thus, given Moren's teaching of various factors that must be considered when attempting to make an aerosol formulation of a poorly water-soluble drug, and that it is highly preferable to utilize water-soluble drugs in aerosol formulations, at the time the claimed invention was made there was no apparent reason to combine the prior art to make an aerosol formulation of a poorly water-soluble drug as presently claimed.

Claim 45 is cancelled, thus rendering all rejections moot with respect to that claim.

B. ***Liversidge, in view of Gennaro and Dieter Kohler***

Claims 28-40, 42-45 and 47-59 are as allegedly obvious over Liversidge in view of Gennaro and Dieter Kohler. In particular, the claims are rejected because "[i]t would have been obvious . . . to prepare the method of delivering an aerosol to lungs as claimed for treatment of respiratory diseases by the combined teachings of the above cited references, because Liversidge et al teaches the average particle size, surface modifier, and all other limitations of the presently claimed invention and Gennaro and Kohler references teach the use of aerosols for poorly soluble drugs and inhalation products and treatment of asthma and other respiratory illness." Office Action at 18-19. Applicants respectfully traverse this ground for rejection.

Kohler only generically describes aerosol formulations and is silent on the issue of inhaled particle size. Nothing in Kohler gives any indication or reason that one would want to make a nanoparticulate formulation of a drug and aerosolize it. In fact, Kohler teaches away from aqueous aerosols containing drug nanoparticles. The last sentence on page 310 (before Figure 3) states that "the water solubility of the drug and its viscosity determine the amount of drug available in the aerosol droplet after nebulization." This statement implies that the drug must be in solution to be suitable for nebulization as an aqueous aerosol. Accordingly, one of skill in the art would have no apparent reason to combine Liversidge and Gennaro with the teachings in Kohler to make an aerosol formulation containing a nanoparticulate drug.

Furthermore, Gennaro deals exclusively with aerosol formulations that contain propellants (specifically fluorocarbons, which are no longer in use). Although Gennaro does make brief reference to "Dispersions or Suspensions (Powder Aerosols)," Gennaro states that "the moisture content should be kept below 300 ppm and the propellants and solvents must be dried by passing them through a drying agent." Gennaro at 1672. Accordingly, Gennaro does not provide any reason to aerosolize aqueous suspensions.

And with respect to Kohler, his only reference to aerosolization of solid particles is on p. 311, where he discusses delivery of solid particles from pressurized MDIs and powder inhaler systems. Accordingly, there is no suggestion that solid drug particles can be delivered by nebulization of aqueous suspensions.

CONCLUSION

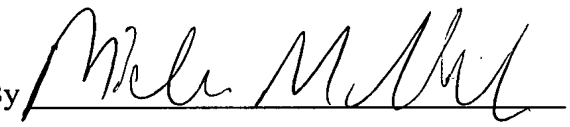
Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is authorized to charge any unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date August 2, 2007

By 

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